

AMENDMENTS TO THE SPECIFICATION:

Please delete the paragraph on page 6, line 5 and replace it with the following paragraph:

The human peptide sequence of HARP₁₃₆ is also presented in sequence SEQ ID N° NO: 1.

Please delete the paragraph on page 6, lines 20-25 and replace it with the following paragraph:

In a preferred manner, the fragments 13-39, 65-97 or 111-136 are the fragments as enumerated in the sequence SEQ ID N° NO: 1, namely the sequences :

13-39 : SDCGEWQWSVCVPTSGDCGLGTREGTRT (SEQ ID N° NO: 2)

65-97 : AECKYQFQAWGECDLNTALKRTGSLKRALHNA (SEQ ID N° NO: 3)

111-136 : KLTKPKPQAESKKKKKEGKKQEKMLD (SEQ ID N° NO: 4).

Please delete the paragraph on page 8, lines 30-31 and replace it with the following paragraph:

The fragments of SEQ ID N° NO: 2 and SEQ ID N° NO: 3 containing respectively the unit 18-23 WQWSVC (Residues 6-11 of SEQ ID NO: 2) or the unit 71-77 FQAWGEC (Residues 7-13 of SEQ ID NO: 3) are of particular interest.

Please delete the paragraph on page 11, lines 1-5 and replace it with the following paragraph:

The nucleic acid which is useful for the production of recombinant peptide can in particular have the following sequences:

- sequence coding for the peptide 13-39 (SEQ ID N° NO: 5)
- sequence coding for the peptide 65-97 (SEQ ID N° NO: 6)
- sequence coding for the peptide 111-136 (SEQ ID N° NO: 7).

Please delete the paragraphs on page 11, lines 10-20 and replace them with the following paragraphs:

These nucleic acids can be defined as comprising :

- i) sequences similar to at least 70 %, preferably at least 80 %, preferably at least 90 %, even at least 95 % of the sequence SEQ ID n° NO: 5, n° SEQ ID NO: 6 or n° SEQ ID NO: 7 ; or
- ii) sequences which hybridise with the sequence SEQ ID n° NO: 5, n° SEQ ID NO: 6 or n° SEQ ID NO: 7 or its complementary sequence under strict hybridisation conditions, or
- iii) sequences which code for the reference peptide as defined above.

In a preferred manner, such a homologous nucleotide sequence hybridises specifically with the complementary sequences of the sequence SEQ ID n° NO: 5, n° SEQ ID NO: 6 or n° SEQ ID NO: 7 under strict conditions. The parameters defining the conditions of strictness depend upon the temperature at which 50% of the paired

strands separate (Tm).

Please delete the paragraph on page 12, lines 6-10 and replace it with the following paragraph:

Therefore a homologous nucleotide sequence includes any nucleotide sequence which differs from the sequence SEQ ID N° NO: 5, N° SEQ ID NO: 6 or N° SEQ ID NO: 7 by mutation, insertion, deletion or substitution of one or more bases, or by the degeneracy of the genetic code, in so far as it codes for a peptide having the biological activity of the fragments of HARP to which they refer.

Please delete the paragraph on page 17, lines 21-24 and replace it with the following paragraph:

A preferred pharmaceutical composition comprises :

- the peptide 13-39 of sequence SEQ ID N° NO: 2 ;
- the peptide 65-97 of sequence SEQ ID N° NO: 3 ; and
- the peptide 111-136 of sequence SEQ ID N° NO: 4.

Please delete the paragraph on page 18, lines 5-9 and replace it with the following paragraph:

A preferred composition comprises:

- a nucleic acid coding for the peptide 13-39 of sequence SEQ ID N° NO: 2 ;

- a nucleic acid coding for the peptide 65-97 of sequence
SEQ ID N° NO: 3 ;

- a nucleic acid coding for the peptide 111-136 of sequence
SEQ ID N° NO: 4.

Please delete the paragraph on page 25, lines 19-29 and replace it with the following paragraph:

Fibroblast cells of type NIH 3T3 are cultured at a density of 3×10^4 cells per cm^2 in DMEM culture medium supplemented with 10% of foetal calf serum. After 24 hours of incubation at 37°C in an atmosphere containing 7 % of CO_2 , the culture medium is replaced by DMEM which does not contain foetal calf serum. Twenty-four hours afterwards, the HARP molecule (4 nM) in the presence or absence of the HARP peptides 16-48 or 65-97 of respective sequences SEQ ID N° NO: 2 and n° SEQ ID NO: 3 at a concentration ranging from 0.1 to 10 μM is added over 18 hours. After this period of incubation, 0.5 μCi of [*methyl-³H*]thymidine is added and 6 hours afterwards the cells are fixed by a 10% solution of trichloroacetic acid. The radioactivity incorporated by the cells is then counted by liquid scintillation after having effected a cell lysis with a solution of sodium hydroxide at a concentration of 0.1 N.

Please delete the paragraph on page 26, lines 11-20 and replace it with the following paragraph:

The capacity of the peptide P111-136 (SEQ ID N° NO: 4) to inhibit tumour angiogenesis has been tested by inducing tumour growth by injection of PC3 cells into nude mice in the presence or absence of peptide P111-136. 2×10^6 PC3 cells are injected into groups of 5 nude mice (nude/nude, Laboratoire IFFA CREDO) treated or not by injection in the region of the tumour of 100 μ l per day of a solution of PBS (control group) or by a solution of peptide P111-136 diluted in PBS at a concentration of 5 mg/kg. On day 9, 13, 16, 20, 23 and 27 the size of the tumour is measured with the aid of a calliper gauge. The results are presented in Figure 3 and indicate that the HARP peptide 111-136 used at a dose of 5 mg per kg induces an inhibition of the growth of the tumours.

Please delete the paragraph on page 27, lines 14-22 and replace it with the following paragraph:

MDA-MB-231 cells from human mammary carcinoma are cultured at a density of 3×10^3 cells per cm^2 in a DMEM culture medium containing 10% of foetal calf serum, 0.35% of agar and containing or not containing concentrations of HARP peptides 13-39 and 65-97 (SEQ ID N° NO: 2 and n° SEQ ID NO:3). The cells are cultured in a culture box with 12 wells (35 mm in diameter/well) previously covered with 1 ml of 0.6% agar. The peptides are added into the culture medium every 2 days. After 13 days of incubation in a humid atmosphere at 37°C and 7% CO₂, the colonies having a

diameter equal to or greater than 50 µm are counted. Each point in the experiment is carried out in triplicate and each experiment is repeated three times.

Please delete the paragraph on page 28, lines 1-4 and replace it with the following paragraph:

As HARP is a growth factor implicated in the proliferation and the differentiation of endothelial cells, the inventors have, in the experiment set out below, studied the effect of the HARP peptides 13-39 and 65-97 (SEQ ID N° NO: 2 and n° SEQ ID NO: 3) on the angiogenic activity induced by HARP.